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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

HARTLEY, MICHAEL G

ART UNIT

PAPER NUMBER

1616

DATE MAILED: 08/29/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/806,680

Applicant(s)

CANTRELL, GARY L.

Examiner

Michael G. Hartley

Art Unit

1616

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 29 July 2002.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-20 is/are pending in the application.
- 4a) Of the above claim(s) 14-20 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-13 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All   b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

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***Election/Restrictions***

Applicant's election of Group I in Paper No. 4 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). The elected species (subgeneric) of the two alkyl carboxylate salts and alkyl-CH<sub>2</sub>CONH(CH<sub>2</sub>)<sub>2</sub>- PEG is acknowledged.

After no prior art could be found to reject the claims as directed to the elected species (e.g., the sub-generic species as provided), the claims were examined in view of other species encompassed by bipolar compounds (e.g., phospholipid blends, etc.) in accordance with *Markush* practice (as set forth in the rejections below).

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 7-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 7, the recitation of "inserting a composition" is confusing because it is not clear what the composition is inserted into or what is meant thereby. This rejection can be obviated by changing "inserting" to "administering" or a similar recitation to clarify that the composition is being delivered to the body tissue.

Claims 8-13 fall therewith.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

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Claims 1 and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Unger (US 5,585,112)

Unger discloses a composition for use as an ultrasound contrast agent in methods of imaging comprising microbubbles encapsulating a gas within a shell made from a blend of bipolar compounds having intermolecular hydrophobic regions of mixed carbon length (i.e., phospholipid blends, charged lipid blends, etc.), see abstract, column 20, lines 31+ and the examples, e.g., example 3. Many of the surfactant blends disclosed by Unger (e.g., phospholipid blends of example 3) are within the scope of a bipolar compound, because such phospholipids are bipolar compounds due to their chemical makeup, i.e., phospholipids are known as being bipolar lipids.

Claims 1 and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Klaveness (US 5,536,490).

Klaveness discloses a composition for use as an ultrasound contrast agent in methods of imaging comprising microbubbles encapsulating a gas within a shell made from a blend of bipolar compounds having intermolecular hydrophobic regions of mixed carbon length (i.e., amphiphilic phospholipids and polymer conjugates), see abstract, columns 2-5, lines 1+ and the examples. Many of the shell forming polymer systems disclosed by Klaveness are within the scope of a bipolar compound, because such amphiphiles are bipolar compounds due to their chemical makeup. Klaveness also discloses amphiphiles of formula II in column 5, wherein R10 is a lipophilic group (e.g., an alkyl) and X is a carboxylate, and PEG derivatives, see column 5-7. These amphiphiles are within the scope of the bipolar compounds as claimed.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

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invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over either one of by Unger (US 5,585,112) or Klaveness (US 5,536,490).

Unger and Klaveness disclose a composition for use as an ultrasound contrast agent in methods of imaging comprising microbubbles encapsulating a gas within a shell made from a blend of bipolar compounds having intermolecular hydrophobic regions of mixed carbon length (i.e., phospholipid blends, amphiphilic polymer conjugates, etc.), as set forth above. Unger teaches the use of various shell materials and combinations thereof which are bipolar compounds and are encompassed by the claimed formula, such as, fatty acids of up to 22 carbon atoms which are linked to a polymer (e.g., PEG) via an amide group, see column 22, lines 20-39. Klaveness teaches the use of bipolar compounds having intermolecular regions of mixed carbon length, as encompassed by formulas I and II, see columns 4-5.

Unger and Klaveness fail to specifically disclose (i.e., exemplify) blends of shell materials that encompass the bipolar compounds encompassed by the formula set forth in the claims.

However, both Unger and Klaveness clearly teach that various combinations (or blends) of shell forming materials may be used in the microbubbles to form stable microbubbles which are useful for encapsulating a gas and can be administered safely and effectively as an ultrasound contrast agent (e.g., Unger teach combinations of all taught shell materials, see columns 20-22 and column 29, lines 47+. Klaveness teaches combinations of shell materials, see column 2.

It would have been obvious to one of ordinary skill in the art to use a combination or blend of any of the useful shell forming materials disclosed by either Unger or Klaveness, many of which are encompassed by the claimed formula, because both Unger and Klaveness teach that such shell materials may be used in equivalent manner in combinations or blends to provide a means of encapsulating a gas in a microbubble for a stable, safe and effective ultrasound contrast agent to improve methods of ultrasound imaging.

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**Conclusion**

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael G. Hartley whose telephone number is (703) 308-4411. The examiner can normally be reached on M-F, 7:30-5, off alternative Mondays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jose G. Dees can be reached on (703) 308-4628. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4556 for regular communications and (703) 308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

  
Michael G. Hartley  
Primary Examiner  
Art Unit 1616

MH  
August 28, 2002